

REMARKS

The Office Action mailed November 30, 2005 and the Notice of Non-Compliant Amendment of July 31, 2006, have been received and reviewed. Claims 1 through 44 are pending. Claims 5-11, 22-25 and 28-44 are withdrawn from consideration. Claims 1-4, 12-21, 26 and 27 stand rejected. Applicants have amended claims 1-4, 6, 7, 12, 15, 16 and 21 without prejudice or disclaimer. Claims 13 and 14 have been canceled without prejudice or disclaimer. New claim 45 was added, but no new matter was added. Reconsideration is respectfully requested.

Notice of Non-Compliant Amendment

A Notice of Non-Compliant Amendment was received because new claim 45 was not a clean copy. Applicants have submitted new claim 45 in clean form and request reconsideration and withdrawal of the non-compliant amendment.

Interview Summary

Applicants are extremely grateful for the courtesy extended by the Examiner during the interview. The interview was beneficial in narrowing the issues being discussed. As noted in Interview Summary, the parties "Discussed in general the rejections of record and explored ways to overcome them. Examiner will consider Applicants' amendment and arguments." Applicants' agree that this summary accurately and completely described the substance of the interview. Should the Office have further questions on this issue, Applicants will provide the requested response.

35 U.S.C. §112, first paragraph

Claim 12 stands rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse the rejection.

Applicants have amended claim 21 to recite "The method according to claim 1, further comprising introducing a vector further comprising an IRES site for insertion of the IRES site by homologous recombination into the glial progenitor cells." Support for this amendment can be found throughout the as-filed specification, including, for example, FIG. 4 and related text.

Reconsideration and withdrawal of the rejection is requested.

35 U.S.C. §102

Claims 1-4, 12-13, 15-17 and 19-20 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Capecchi et al. (U.S. Patent 5,631,153) as evidenced by Sedivy, J.M. (Proc. Natl. Acad. Sci. USA 95:9078-9081 1998).

Claims 1-4, 12, 15 and 16 have been amended to recite “glial progenitor cells” rather than “stem or progenitor cells.” Support for this amendment can be found throughout the as-filed specification, including, for example, claim 14. The Examiner acknowledged that Capecchi et al. fails to teach the preparation of homologous recombined glial progenitor cells. (Office Action, page 8). As Capecchi et al. fails to disclose every element of the presently claimed invention, it cannot anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection is requested.

Claims 1-3, 12, 15 and 16-17 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Economides et al. (U.S. 2003/0003581) as evidenced by Sedivy, J.M. (Proc. Natl. Acad. Sci. USA 95:9078-9081 1998).

Economides et al. discloses a method of homologous recombination in embryonic stem cells. Economides et al. does not disclose a “method of obtaining homologous recombination in glial progenitor cells” as recited in the presently claimed invention. As Economides et al. fails to disclose every element of the presently claimed invention, it cannot anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection is requested.

35 U.S.C. §103

Claims 1, 13-14, 19 and 26 stand rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Capecchi et al. (U.S. Patent 5,631,153) in view of Rao et al. (U.S. Patent 6,235,527).

As discussed at the interview, the Examiner acknowledged that Capecchi et al. fails to teach or suggest the preparation of homologous recombined glial progenitor cells as recited in the presently claimed invention. (Office Action, page 8). Applicants respectfully disagree that it would be obvious to modify Capecchi et al. by genetically modifying an isolated pure population

of mammalian central nervous system glial restricted precursor cells of Rao et al. by homologous recombination. As discussed at the interview, Rao et al. discloses methods of introducing genetic material into cells. However, Rao et al. lacks any teaching or suggestion of introducing a gene to a particular locus or retaining DNA at a specific site, which is necessary for homologous recombination.

Further, neither reference teaches or suggests homologous recombination in glial progenitor cells and the use of homologous recombination in glial progenitor cells would not be obvious. For years, homologous recombination in somatic stem and progenitor cells has been impossible because of challenges with propagation, selection and vector selection. *See, e.g., Specification*, paragraphs [0008]-[0011].

Glial progenitor cells are distinct from neural stem cells, in particular, and all stem cells in general. Progenitor cells (including glial progenitor cells) are restricted precursors of stem cells. “During differentiation, stem cells may generate more restricted precursors (also known as “progenitor” cells) which can undergo limited self-renewal but have a more restricted repertoire of differentiation. Glial progenitor cells, for example, can differentiate into multiple types of glial cells (*i.e.*, astrocytes and oligodendrocytes) but not into neurons, while neuronal progenitors can generate multiple types of neurons but not astrocytes or oligodendrocytes.” Specification, paragraph [0005].

Further, glial progenitor cells have a more limited self-renew potential, more limited ability to differentiate, and differ in marker expression and growth factor requirements than stem cells. These criteria have been used to uniquely define and distinguish glial progenitor cells from neural epithelial stem cells and other stem cell populations. *See, e.g., Rao, “Multipotent and Restricted Precursors in the Central Nervous System” The Anatomical Record, 257:137-148 (1999) and Rao et al., “Precursor cells for transplantation” Progress in Brain Research, 128: 273-294 (2000).* (Copies of which are provided herewith). Thus, Capecchi et al.’s general disclosure of neural stem cells cannot anticipate or render obvious the use of glial progenitor cells in the presently claimed invention.

Capecchi et al. includes a laundry list of potential cell types, but notably omits glial progenitor cells from the disclosure, which suggests that Capecchi et al. did not believe glial progenitor cells were a viable candidate for homologous recombination. Indeed, in the interview,

the Examiner acknowledged Capecchi et al.'s lack of disclosure of glial progenitor cells.

The ability to perform homologous recombination in glial progenitor cells was not obvious from either Rao et al. or Capecchi et al. and is dependent on a later discovery that glial progenitor cells can be made to self-renew for prolonged time periods by exposure to a combination of growth factors and that glial progenitor cells do not undergo senescence as they express high levels of telomerase. This unique combination of features distinguish glial progenitor cells from all other somatic cell populations and allow one to perform homologous recombination in this population. Neither Capecchi et al. nor Rao et al. predicts that glial progenitor cells express telomerase, or suggest that glial progenitor cells can be used for homologous recombination.

As the proposed combination of references fails to teach or suggest every element of the presently claimed invention, Applicants respectfully submit the current claims are not rendered obvious by Capecchi et al. in view of Rao et al. Reconsideration and withdrawal of the rejection is requested.

Claims 1 and 26-27 stand rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Capecchi et al. (U.S. Patent 5,631,153) in view of Rao et al. (U.S. Patent 6,235,527) as applied to claims 1, 13-14, 19 and 26, and in further view of Weiss et al. (U.S. Patent 5,570,376).

The discussion of Capecchi et al. and Rao et al. are incorporated herein. Weiss et al. fails to cure the deficiencies of Capecchi et al. in view of Rao et al. None of the references teaches or suggests homologous recombination in glial progenitor cells and the use of homologous recombination in glial progenitor cells would not be obvious. For years, homologous recombination in somatic stem and progenitor cells has not been possible because of challenges with propagation, selection and vector selection. *See, e.g.*, Specification, paragraphs [0008]-[0011].

As the proposed combination of references fail to teach or suggest every element of the presently claimed invention, Applicants respectfully submit the current claims are not rendered obvious by Capecchi et al. in view of Rao et al. in further view of Weiss et al. Reconsideration and withdrawal of the rejection is requested.

Claims 1 and 15-18 stand rejected under 35 U.S.C. §103(a) as being allegedly

unpatentable over Capecchi et al. (U.S. Patent 5,631,153) in view of Steeg et al. (Proc. Natl. Acad. Sci. USA 87:4680-4684, 1990).

The Examiner acknowledged that Capecchi et al. fails to teach or suggest the preparation of homologous recombined glial progenitor cells as recited in the presently claimed invention. (Office Action, page 8). Steeg et al. fails to cure the deficiencies of Capecchi et al. as Steeg et al. teaches the use of embryonic stem cells, not glial progenitor cells as recited in the presently claimed invention. (Steeg, page 4680, right column). As the proposed combination of references fail to teach or suggest every element of the presently claimed invention, Applicants respectfully submit the current claims are not rendered obvious by Capecchi et al. in view of Steeg et al. Reconsideration and withdrawal of the rejection is requested.

New Claim

New claim 45 avoids the cited references at least for the same reasons as claim 1. No new matter was added. Support for new claim 45 can be found throughout the as-filed specification including, for example, claims 1, 2 and 14.

Conclusion

Claims 1-4, 12, 15-21, 26, 27 and 45 are believed to be in condition for allowance, and an early notice thereof it respectfully solicited. Should the Office determine that additional issues remain which might be resolved by a telephone conference, the Examiner is invited to contact Applicants' undersigned attorney.

Respectfully submitted,



Krista Weber Powell
Registration No. 47,867
Attorney for Applicants
TRASKBRITT
P.O. Box 2550
Salt Lake City, Utah 84110-2550
Telephone: 801-532-1922

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